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In This Issue

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Medical Research Mission to the Soviet Union: Part II

A. Baird Hastings and Michael B. Shimkin

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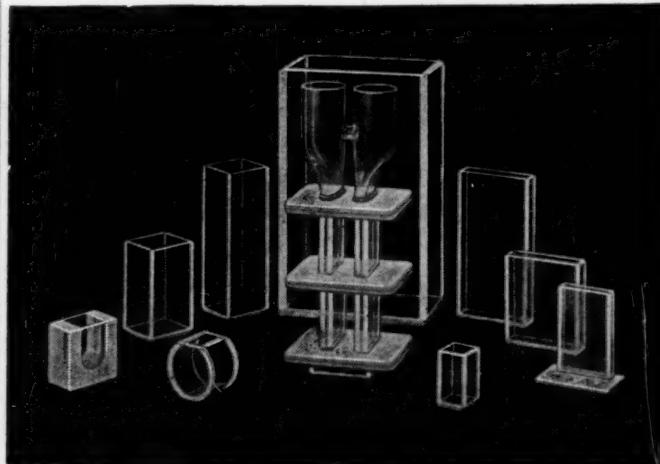
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SCIENCE

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Friday, May 24, 1946

Medical Research Mission to the Soviet Union: Part II

A. Baird Hastings and Michael B. Shimkin

THE VISIT TO RUSSIA of the authors, together with Sir Howard W. Florey and Dr. A. G. Sanders of Oxford, during January and February 1944 for the purpose of discussing problems in medical research with Russian medical scientists, related in *Science*, 1946, 103, 605, resulted in numerous contacts with individual investigators in their laboratories. This second installment is an account of visits to the principal laboratories and hospitals during our stay in Moscow.

BLOOD TRANSFUSIONS AND BLOOD SUBSTITUTES

The Soviet Union developed a sound, efficient blood-supply system for its needs during the war (9). The Central Institute of Hematology and Blood Transfusion, directed by A. A. Bagdasarov, has 6 affiliated institutes, 72 large collecting stations, and small collecting stations and points numbering over 400 and covering the country from Archangel to Rostov. The Central Institute averaged 750 blood collections per day, and 860 tons of blood had been supplied to the Army by 1944.

The donors are examined and typed, and a serologic test for syphilis is done at district posts. After being sent for according to requirements, they undress, put on clean caps, gowns, and trousers that include the feet, and proceed to the surgical rooms which are divided according to the type of donor's blood. Donors of only one blood type are admitted to any one room. Blood donors receive a meal and are eligible for special food rations. It was stated that 250 cc. of blood is taken from the donors the first time and 450 cc. of blood at succeeding visits, with at least a six-week interval between bleedings.

The blood is collected in long vials of 250 cc. with 10 cc. of 25 per cent glucose and 10 cc. of 5 per cent citrate. This mixture can be sterilized within the bottle at pH 4.9. The blood is sealed immediately by compression of an attached rubber tubing, and the cut end is dipped in paraffin and sealed. A final typing of the blood is done at this time as a final check.

The whole blood is kept at 2-6° C., and transported

in special boxes by airplane to the front. The Army orders blood in anticipated amounts and for areas needed in their operations. The transport, delivery, and handling of the blood are done by one organization called the "OPK." Blood is used up to 25 days after collection, but seldom remains unused for that long.

At the time of our visit over 80 per cent of the blood collected was supplied to the Army in the form of whole blood. Approximately 20 per cent of the blood was processed and distributed as plasma or serum. Serum was preferred to plasma because a clearer product was obtained.

During the winter of 1941-42, three tons of frozen serum were sent to the front. It was frozen rapidly by the simple expedient of setting it out on the snow. In thawing, the serum is placed in tepid water and the temperature raised to 38° C. within 12 minutes. Dried plasma and serum were obtained by vacuum at room temperature after the addition of 40 cc. of 25 per cent glucose per liter. The ampoule of dried material is connected directly with an ampoule of distilled water, so that reconstitution of the plasma or serum is achieved by opening the connection; solution occurs in 10-15 minutes.

Plasma and serum are drawn off from blood cells after the blood has stood in the cold for four days. They are kept at room temperature for another seven days in a container with a test-tube extension which can be sealed off from the main container and the contents used for bacteriologic and other test purposes.

Other solutions used in transfusion are variations of salt solutions (1), except one in which "nonantigenic" casein is used. It was stated that the casein was extracted with alcohol and that materials to which are attributed antigenic properties were thereby removed. We were informed that they have tried this material in 300 cases, without untoward results when up to 30 grams of casein were used, and without reaction upon repetition, although some cases received up to five repeated infusions. The infusion was stated to be efficacious in cases of hypoproteinemia and

shock, but had not been tried in burns. It was also reported to stimulate blood cell production and antibody formation.

Interesting "anesthetic solutions," containing hydrocodeinone and ephedrin, and a solution containing alcohol stated to be useful in shock, were also demonstrated.

At the Sklifasovski Hospital, S. S. Yudin reported on his experiences with cadaver blood. During 1935-43, 2,964 cases were bled, 5,092 liters of blood being obtained. Of these, 1,331 liters had to be discarded due to hemolysis, infection, positive serology, or other causes. The average yield from a body was 1.6 liters when bled from the jugular vein only and 3.0 liters when the femoral vein was also drained. Collection of blood must be carried out within three to four hours after death during the summer and within six to eight hours during the winter. Sulfanilamide in 0.8 per cent concentration is added to the blood obtained. The method is impractical for use at the front, but the cadaver blood bank supplied the needs of the hospital.

TYPHUS VACCINE

The Soviet Union was using mouse-lung typhus vaccine, and this product was demonstrated and discussed by M. K. Krontovskaya at the Central Institute of Microbiology and Epidemiology.

The mice are given rickettsia intranasally. The lungs are removed on the third or fourth day after inoculation, ground with quartz, and centrifuged at 1,500 r.p.m. for five to eight minutes; this removes the quartz and the gross lung tissue. The preparation is then centrifuged at 4,000 r.p.m. for two hours, which throws down the rickettsia. Suspensions of rickettsia are emulsified with formalin, 0.2 per cent, to form the vaccine. Use is made of a standard of 1,000 million rickettsia/cc. (800 to 1,200 million/cc. is the allowable fluctuation), which is determined by optical comparisons of each batch with a standard and actual counts.

The Soviet scientists and epidemiologists were reported to be satisfied with the mouse-lung preparation. The main advantages were stated to be the simplicity of its preparation and the uniformity of the material obtained. Among the main objections to the egg vaccine were the sharp, apparently unpredictable drops in the number of rickettsia in some batches of eggs. The main disadvantage of the mouse-lung preparation was the danger of laboratory infection.

Krontovskaya described and later demonstrated interesting morphological differences in rickettsia isolated from mouse lungs at different intervals after inoculation. Two days after inoculation, the rick-

ettsia appear as long, thin, faint, extracellular organisms; in three to four days the organisms begin to assume the small, oval shape usually seen, and in five days the forms are tiny and appear as if they have been fragmented. Reinoculation of these very small forms, however, results in the presence of the long, thin forms in the reinoculated mice, two days after transfer. They consider that the most virulent stage is the long, thin form and therefore sacrifice the mice at about the third day.

Typhus rickettsia is obtained from the blood of human typhus cases. It is passed through lice for three passages, guinea pigs are then injected intraperitoneally with the ground lice for three passages, and the tunica vaginalis fluid is used for inoculation of mice. The culture is then carried on directly as mouse-rickettsia: suspension-mouse transfers.

The schedule of immunization of human beings is three doses of 1 cc. of vaccine at five-day intervals. Immunity is established in one month and lasts for about a year. Booster doses of 0.5 or 1.0 cc. are then given.

In connection with the time after vaccination that protection occurs, the case of a medical group at the front was cited: 22 were vaccinated more than a month before exposure, and none developed typhus. 2 of the group of 24 had just completed their course and both developed typhus, although in a mild form.

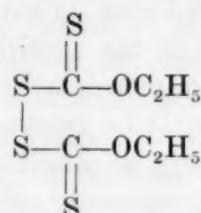
There was conviction that vaccination against typhus is an efficient procedure, although there was still room for improvement. We were shown the results of one large epidemiologic study in which approximately half of 20,000 comparable individuals were vaccinated with the mouse-lung preparation. Among the nonvaccinated group the rate per 10,000 rose to 32.6 during the peak month, and for a month before and after the peak the rate was 25-30. The highest rate in the vaccinated group was 4, and the curve was practically flat throughout the year's period of observation. Beside this reduction in rate there was a marked decrease in the mortality among those contracting the disease: The average hospitalization period in the vaccinated cases was about 1.5 weeks, for the unvaccinated, about 3 weeks. Convalescence in the vaccinated cases took an average of 12 days in comparison to 35 days in the nonprotected individuals.

Experimentation with egg vaccine and louse vaccine was being carried out by Krontovskaya and by Smorodintzev. An interesting development in the preparation of Weigl's type of vaccine was the use of an artificial feeding chamber devised by Pshenichnov. Skin is removed from fresh cadavers and spread like a drum over a cylinder, citrated blood infected

with rickettsia being pooled underneath. The lice are dropped on this drum and soon start sucking; 5 cc. of blood feeds several thousand insects. The lice do not reproduce under these conditions, however, and for maintenance of normal colonies donors still have to be used. The method is widely applicable to the study of diseases involving blood-sucking insects.

INSECTICIDES AND DISINFECTANTS

Apparently the principal insecticidal weapon used by the Soviets against lice and typhus was soap containing a compound designated as "preparation K." The active principle of "K" is bisethylxanthogen:



This compound is combined at 50 per cent strength with soap. Preparation K, emulsified with soap, kills lice on contact within six to eight hours, although it paralyzes them sooner. It is also used (20 grams/liter of water) to impregnate clothes. The impregnation is done in special cylinders and is retained in the clothes for at least a month. However, it does not withstand laundering. The main drawback of the material is its onion-like odor.

Since K is difficult to make into a powder, another product, "SK," is used mixed with tale. SK is a chlorinated turpentine, mixed in a 50-50 ratio with an emulsifying agent, and this is mixed with some base such as tale to produce a powder containing 10-20 per cent of SK. The preparation kills lice in six to eight hours. It is not malodorous. Another insecticidal powder, highly but slowly lousicidal, is "DFA," diphenylamine mixed at 25 per cent concentration with tale.

Among insect repellents, use had been made of eugenol (4-allyl-guaiacol) as an impregnating material for nets. To impregnate external clothing against ticks and flying insects a preparation known as "8502" was also used. It consisted of 25 per cent of tetrachlorphenol, 25 per cent of para-oxychlordiphenyl, and 50 per cent emulsifier. Anabasine sulfate, a plant product, was also considered favorably as an insect repellent (5).

A newly adopted method of general disinfection, particularly of water, was described. It is based on the use of chlordioxide, ClO_2 , which is unstable; the problem was to stabilize it and then to develop means of liberating chlordioxide easily and simply. Stabilization was effected by using a metal salt of chlordioxide, combined with 50 per cent NaCl and 1 per cent

$\text{Ca}(\text{OH})_2$. This mixture was entitled "Neopantocid." The agent that will liberate ClO_2 is called the "Katalizator" and consists of $\text{Na}_2\text{S}_2\text{O}_7$ mixed with 1 per cent Fe_2SO_4 . This product, to differentiate it from the Neopantocid, is colored gray by the addition of carbon particles.

To use the material, 1 gram of Neopantocid is mixed with 1 gram of the Katalizator, and a little water is added. A brown liquid that turns to yellow is formed, due to liberation of chlorine. The mixture has 250 mg. of ClO_2 and is mixed with water to produce the desired concentration. ClO_2 is strongly bactericidal, 100 mg./liter killing all spores, including anthrax, in five minutes. In comparison, while 20 mg. of ClO_2 kills anthrax spores in two hours, 1,000 mg. of Cl_2 does not do so.

ANTIBIOTICS

The Department of Biochemistry of Microbes and Immunity, directed by Z. V. Yermolieva, was studying the problem of antibiotics and related phenomena. Work on penicillin and on gramicidin was based on the publications from British and American sources.

Bacteriophage. Since bacteriophages purified by electrophoresis are protein free and have no respiration, either aerobic or anaerobic, they conclude that phages are nonviable. Phages can be prepared from apples, onions, and carrots, and have been used clinically in the treatment of colitis.

Dysentery phage is prepared in either liquid or solid form, the latter obtained by the electrospray drying method at -40°C . For prophylaxis, a phage-lysate of dysentery organisms is used, 1 cc. containing one billion lysed organisms. The first dose of 1 cc. is given subcutaneously. After two weeks a series of 15-cc. doses are given orally at intervals of three to four days. For active bacillary dysentery, phage treatment is combined with sulfathiazole or with egg lysozyme, given orally. It was stated that the lysozyme was useful in allaying vomiting. For chronic dysentery a combination of phage and lysozyme was stated to promote healing of intestinal ulcerations. For infantile diarrheas phage is used with nicotinic acid, said to enhance the titer of the phage.

Wound phages for pyogenic organisms are used in conjunction with sulfapyridine or sulfanilamide. For necrotic wounds, phage and lysozyme are used, the latter assisting in the removal of sloughs.

Cholera phage is also being tried, and experimental work is being carried out on monkeys at Tashkent.

Lysozyme. Egg lysozyme is used mainly, but lysozyme is also prepared from horse-radish and turnips. It was stated to be bactericidal to streptococcus and staphylococcus, and bacteriostatic for dysentery, typhoid, and cholera.

Clinically it is used for wounds, especially of the cornea, and for preparation of wound beds before skin grafting. In mustard-gas burns it has no specific effect but does reduce secondary complications.

Industrially a crude preparation is used in the processing of caviar. The fish eggs are washed in a solution of 1/1,000,000 and remain fresh for a year. A similar crude preparation is used for soaking flax, the fibers of which can then be separated after only 40 hours of soaking instead of 10 days when plain water is used.

Gramicidin. An active strain of gramicidin-producing bacteria was isolated from the sludge of a slow stream at Tashkent. The organisms differ from the *B. brevis* used by Dubos, and the product is reported to differ from the American gramicidin (4). A tryptic digest method is used in the separation of gramicidin. It is supplied in 0.5-cc. ampoules containing 4 per cent gramicidin dissolved in alcohol.

Penicillin. Ninety-three strains of mold, gathered mostly from damp air-raid shelters, were investigated. It was found that one culture, identified as *Penicillium crustosum*¹ by their mycologists, was an active antibiotic producer.

The mold is grown in large, flat bottles on a Czapek-Dox medium containing 8 per cent yeast extract; glucose rather than lactose is used. After four to seven days of incubation, the brew is filtered through paper in a Seitz filter and then through Chamberland candles. It is ampouled directly from the pooling bottles without further purification, and this product is used clinically. The ampoules are stored in a refrigerator and potency maintained for about two months.

Standardization is done by testing the potency against their own culture of *Staph. aureus*. For the most part, tube dilution procedures are used, although it is referred to as the Oxford method. By this method of assay the brew of the mold contained approximately 100-120 units (Soviet)/cc. Monthly production averaged 200 liters (20 million Soviet units), although in December 1944 they produced 500 liters.

Mouse protection experiments were carried out by injecting the animals with staphylococci and penicillin simultaneously in the axilla. Twenty-four hours later, the animals were killed and the axillary lymph nodes cultured. Staphylococci were isolated only from the control animals that received the organisms without the drug.

Penicillin of their production had been used clinically on 179 cases of sepsis and infected wounds, and all were seriously ill. Of these, 160 recovered, 7 died, and no effect was noted in 12. The drug was

¹ A sample of this mold presented to us by Prof. Yermoljeva was later identified by R. D. Coghill, of the Regional Laboratory at Peoria, as *Penicillium notatum*.

given intravenously or intramuscularly in 10-cc. doses and no toxic symptoms have been noticed other than a pyrogenic reaction when 40 cc. are used. Most of the patients received 10,000-50,000 Soviet units of penicillin.

Tests performed by Drs. Florey and Sanders of the Soviet penicillin brew assayed at 30 to 40 units/cc. by the Oxford method. Although a culture of the mold was identified as *P. notatum* in America, the product is apparently somewhat different (7).

SURGICAL PROBLEMS

The principles used in the treatment of shock and wounds in the Soviet Union do not differ significantly from those followed in the United States.

Shock. The main principle in the treatment of shock is organizational: *i.e.* treatment of the casualty is carried out as early as possible. Their policy is not to treat wounds, especially extensive wounds, for the first half hour, but to concentrate on shock. This is then followed by surgical treatment of the wound.

At the Physiology Institute of the Academy of Sciences, Lena Stern described the treatment of shock by the intracisternal injection of potassium phosphate. None of the Soviet surgeons in Moscow of whom we made inquiry used this method of treatment.

Wounds. The main principles in the treatment of wounds are: (1) rapid and adequate surgical interference, (2) use of bactericidal and bacteriostatic agents, particularly sulfonamides, and (3) correct immobilization, including plaster casts. Plaster casts were used for soft-tissue wounds as well as for fractures.

The bacterial flora of wounds is always multiple. In secondary operations and in chronic wounds the procedure is to clean up the wound with sulfonamides and, if necessary, to graft early. Tetanus is not a problem due to active immunization, but the sera against gas gangrene are still considered as not adequate.

Burns. Burns are treated as extensive wounds. These cases are not approached without masks, talking is kept at a minimum, and asepsis is rigidly observed. No local anesthetics are used; soap and ammonia are used to clean the burn, and it is covered with dry dressings, not pastes. However, in second-stage burns the Russians had not given up tannic acid and silver nitrate, as they have seen no bad results if sterile precautions are maintained. Tanning is, of course, not used on hands, genitalia, or face. A well-fitting plaster cast is of great importance in these cases. In third-stage burns, early skin grafts are of primary importance.

Frostbite. It was stated that some surgeons pre-

ferred the rapid, others the slow, thawing method in treating frostbite. Spassokukovsky advocated the injection of procaine into the artery leading to the affected part. It was stated that the method was not dangerous and the results good. The procedure relieved the spasm of the vessels and was used in combination with slow thawing. During the Finnish War ultraviolet radiation was used with good results in the second and third stages of frostbite; this promoted separation of gangrenous parts, and hospitalization was not longer than following amputation.

Neurosurgery. The main problem in infected brain injuries was how to combat the complicated mixture of contaminating bacteria associated with such wounds. Of bacteriostatic agents, combinations of sulfanilamide, sulfathiazole, and sulfapyridine were used in the form of emulsions. Grashchenkov had obtained American gramicidin and used it with gratifying results on 250 cases, in half of which the brain was grossly infected and in half of which gramicidin was used prophylactically. Against gram-positive cocci, it was superior to sulfonamides and stimulated the formation of granulation tissue. The only untoward effect noted was bleeding from exuberant granulations if gramicidin was used too freely.

Grashehenkov used nerve grafts preserved in formalin in about 100 cases of peripheral nerve injury. No positive results were seen in nine months, and histologic examination of some cases showed that nerves had not grown through the graft but under and around it. He was using fresh nerve or tannin transplants from the patients themselves in order to bridge the gap for possible nerve regrowth. The results of this procedure were not yet available.

At the hospital of the First Moscow Medical Institute it was reported that intracarotid injection of sulfapyridine was effective in meningitis, meningoencephalitis, and brain abscess. Up to 20 cc. a day of a 10-per cent solution of sulfapyridine in 50 per cent glucose is injected slowly into the common carotid artery. The injections are carried out without skin incision and are easily repeated. In experimental observations on dogs a level of 28 mg./100 cc. of cerebrospinal fluid was reached within 15 minutes. Such concentrations cannot be obtained with intravenous injections. They showed charts of several patients who received the injections for three to six days; the temperature and pulse returned to normal within a few days, and it was stated that they recovered. No statistics were presented as to the incidence of recoveries or on the complications arising from the procedure.

In brain abscesses the above procedure is used pre-operatively. This is claimed to help sterilize and

wall off the abscess. The abscess is localized before operation by ventriculograms, which give the approximate location. A needle is then introduced into the abscess, and the contents drawn off and replaced by air to outline the space in relation to the ventricles. The operation then proceeds in an attempt to remove the abscess with its capsule.

Chronic wounds. At the Botkin Hospital, gramicidin of Soviet preparation had been used in about 300 cases of chronic infected wounds, and also in some 500 cases prophylactically. The 0.5-cc. ampoule containing 4 per cent gramicidin is mixed with 50 cc. of water for use and applied topically, preparatory to plastic repair. No local toxic reactions had been seen other than occasional bleeding from clean granulating surfaces if treatment is prolonged. No general toxicity had been observed no matter how large the treated surface area was or in cases where the wound was fresh and bleeding. It was also used in empyema, except that of tuberculous etiology, the gramicidin being injected into the pleural cavity after evacuation of the pus.

The course of an infected wound is followed by cleansing the wound of pus and superficial necrotic tissue and making impressions of the surface upon sterile slides that are dropped on and removed without sliding over the tissue. The preparations are stained with Giemsa. The first picture of the infected wound impression is: almost a solid smear of polymorphonuclear leucocytes and many extracellular bacteria. Upon a favorable defense reaction, there are fewer leucocytes and a gradual increase in the number of phagocytosed bacteria. This phenomenon parallels the phagocytic power of leucocytes in peripheral blood, as measured upon exposure of blood *in vitro* to a standard staphylococcus culture. With continued healing, bacteria disappear first, followed by a gradual decrease in the number of leucocytes and appearance of large monocytes. The last favorable stage is the appearance of profibroblasts and fibroblasts, *i.e.* beginning connective tissue-reaction and healing. Reversal of the trend is indicative of worsening of the process, and the observations are used as an index to treatment measures and prognosis. A whole series of impressions are taken if the wound is extensive, and impressions are taken with every change in dressings (6).

Wound dystrophy. At the Department of Physiological Chemistry, VIEM, directed by Academician J. O. Parnas, Prof. Kaplansky was studying protein metabolism in cases of wound dystrophy. This syndrome assumed grave importance during the war. Two or three weeks after severe wounding, a certain percentage of patients develop hypoproteinemia. It

is believed that this is due to excessive breakdown of proteins as well as to deficient synthesis. In the early stages the urinary nitrogen excretion is markedly elevated, and with exhaustion it is markedly reduced. This metabolic picture resembles that seen in rats in which hypoproteinemia is developed by maintenance upon a 6-per cent protein diet. The type of wound in these cases is not of primary importance, the main factors being severity and nonhealing; sepsis is not necessarily present, although often it complicates the picture. They have seen many cases in which the total blood proteins were 2-3 grams/100 cc. There is, of course, an associated hypochromic anemia, edema, wasting, etc. At autopsy the most striking finding, other than the usual manifestations of cachexia, is the peripheral type of necrosis and hemorrhage in the liver with marked vacuolization of the viable hepatic cells.

Kaplansky was treating these cases with trypsin and pepsin digests of proteins and reported that they were beneficial in some cases. He was able to save several patients who had been despaired of, including one man who had a serum protein level of 1.75 gram per cent; after prolonged treatment the patient was maintaining a level of 7.5 gram per cent. It was considered important to supply the sulfur-containing amino acids, cysteine or methionine; the addition of glutathione was suggested as desirable. The amino acid digests were injected intravenously in concentrations of 10 to 20 per cent by weight in 350-500 cc. of liquid. The infusions were given within an hour, since their patients did not tolerate infusions lasting four hours. It was claimed that, except for occasional vomiting, there were no reactions other than occasional slight rises in temperature and headache.

Restorative surgery. Among surgical operations described were Yudin's total gastrectomies and reconstructions of the esophagus, Frumkin's plastic operations on the genitourinary organs, and the radical resections of septic shoulder and leg joints. Some of the work of Yudin and of Frumkin has been reported in the American literature (2, 8).

Operations of the joints were demonstrated at the Botkin Hospital. In the shoulder operation the whole joint, part of the humerus, and the clavicle and scapula may be removed in cases that do not respond to chemotherapy and are obviously septic. In the last 13 cases of resections of the shoulder neither a patient nor an arm had been lost. Two cases were demonstrated; they had a functional arm, although obviously flail-like in motion. X-ray pictures showed thickening of the space between the resected arm and the bone left in the shoulder. The hip operation is obviously more serious. They had done 16 wide resec-

tions, including the whole head of the femur, part of the acetabulum, and part of the shaft. As much as 14-16 cm. of bone may be removed. Two cases died; in two, disarticulation operations had to be performed subsequently. But 14 patients retained their legs and after months, with thickening of the soft tissues in the empty area, can in some measure walk upon this extremity. The results were better than any prosthesis, it was said, but the operation was performed only as a last life-saving resort.

At the First Moscow Medical Institute 70 per cent of the operations are done under local anesthesia, including those on the abdomen and chest. In 10 per cent the local infiltration is reinforced by intravenous evipan, and only 20 per cent of the operations are done under general ether anesthesia. No chloroform is used, and ethylene and cyclopropane were not available. Spinal anesthesia was used rarely at this institution because of personal preferences but is very popular elsewhere.

ACS serum. Inquiries were made concerning the antireticulo-cytotoxic serum of Bogomoletz. None of the clinicians of whom we made inquiry were able at that time to express an opinion of its clinical value from personal experience. We did not have a personal meeting with Prof. Bogomoletz.

INFECTIOUS AND INTERNAL DISEASES

The Red Army received routine immunizations against typhoid, paratyphoid A and B, tetanus, and smallpox. Typhus vaccine is used upon indications of season and geographic area.

Bacteriophage is used widely, particularly in bacillary dysentery, and prophylactically against dysentery and cholera. The preparations are believed to be effective, both prophylactically and therapeutically. Oral tablets, composed of agar media on which the material is grown after killing the remaining pathogens with chloroform, are given every 10 days during the dysentery season in regions where the disease is prevalent. Acetyl sulfaguanidine has been very effective in dysenteries.

BCG vaccine is used widely, and all children are supposed to receive the vaccination. No ill effects have been encountered with this procedure.

In the Soviet Union pneumonias of Types I and II account for 65 per cent of the cases, which was stated to explain their lower mortality as compared with that in the United States. A combined serum and chemotherapy regime was preferred at the Botkin Hospital, with sulfathiazole or sulfadiazine replacing sulfapyridine.

It was stated at the Botkin Hospital that the expected sharp rise in rheumatic fever did not material-

size during the war. Infectious hepatitis or virus pneumonia had not been seen, although they were acquainted with both diseases.

Clinical studies on malaria have been carried out in Middle Asia during the past 20 years. Main reliance in the prevention and treatment of malaria is now placed on quinaerine (atabrine). It was stated that its effectiveness was proportionate to its concentration in blood and particularly in the erythrocytes. For best therapeutic effect, a large primary dose was given intramuscularly as well as by mouth. Usually the drug is given in 2- to 4-day courses with rest intervals of 7 to 10 days, and may be combined with plasmochin. The daily dose, according to the age of the patient, is 0.2 to 0.6 gram. Quinine is used sparingly, in severe cases. Related chemical compounds of the 4-aminoquinoline series had also been investigated (3).

Tularemia vaccine, consisting of heat-killed, glycerinated culture of *B. tularensis*, is used therapeutically as well as prophylactically. Tularemia is not a problem in the USSR except in some regions of Siberia, and recently it had broken out in some reoccupied regions. It was stated that it was transmitted through the oral route due to heavy contamination of food in German storehouses by the feces and urine of infected rats and other rodents. At the Botkin Hospital approximately half of 500 cases of tularemia from the liberated zones were treated with the vaccine. The rationale of using a vaccine therapeutically is that tularemia is a chronic disease and the vaccine might stimulate antibody formation. The vaccine was injected intravenously, in a dose of 50,000 organisms for the first injection. There is a sharp increase in fever, headache, and malaise. Increasing doses for a course of three to six injections are given at three- or four-day intervals. It was stated that the average length of illness with the vaccine was 20 to 30 days, whereas the controls were ill for two to three months. Complications were reduced, and the clinical course was improved.

The number of peptic ulcers has risen markedly during the war. Moreover, there has been a remarkable alteration in the location and sex-distribution since the war. Yudin stated that before the war there were at least three duodenal ulcers for every gastric one; now the ratio is 50:50. Women accounted for 10 per cent or less of the chronic cases; now they constitute 20 per cent. Before the war 90 per cent of the perforations were duodenal, whereas now 50 per cent are gastric; and of these, the rate in women in comparison to men rose from 1.4 to 10 per cent.

NUTRITION AND VITAMINS

At the Institute of the Biology Section, Academy

of Sciences, demonstrations and discussions were held on certain aspects of vitamin sources and nutrition.

The green shell of the walnut was considered an excellent source of vitamin C. Treatment is difficult because of the presence of bitter substances and tannins, but 50 grams of crude extract containing 0.8 per cent ascorbic acid can be obtained from 11 kg. of walnut shells. In the first year of production 500 tons of walnuts were processed this way. Pine needles may be used as a source of vitamin C, but the extract is bitter and the vitamin content disappears within two to three days, although it can be stabilized for a week by fermentation. It was stated that a daily intake of 25 mg. of ascorbic acid per person was the goal toward which they were working.

Work was proceeding on "vitamin K₃," a product obtained from maize tassels extracted with organic solvents. The substance has strong antihemorrhagic action, producing a tenfold reduction in clotting time in rabbits following the intravenous injection of 1 cc., representing about 20 grams of raw material. The effect is most pronounced about 90 minutes following injection. The clotting time is reduced in normal animals as well as in those with K-deficiency hypoprothrombinemia.

It was stated that work on cleavage products of carotene revealed that ionone, instead of being physiologically inactive, has powerful antisympathetic effects. Bovine feces were suggested as a source of carotene, since cattle do not utilize it in appreciable amounts.

Methods of dehydrating vegetables and fruit, use of polar lichen as a source of glucose, and the problem of certain toxic molds in grain were also being investigated. Biochemical experiments on plant genetics, particularly wheat and barley, showed correlation between productiveness and hardness of grain and the catalase activity, and this was used as an index in further crosses between strains to improve the grain.

MISCELLANEOUS OBSERVATIONS

Fundamental research had been continued without marked interruption during the war. Although shortage of technical assistants was reported, recruitment and training of young men and women for scientific research were encouraged.

At the Institute of the Biology Section, Academy of Sciences, V. A. Engelhardt had made important contributions to the chemistry and physiological function of myosin, the mechanism of the Pasteur effect, and on the role of phosphoric acid in photosynthesis. At the Department of Physiological Chemistry, directed by J. O. Parnas, Braunstein was working on thiamine and on the transamination of amino acids; Stepanenko, on the mechanism of glycogenesis and

glycolysis; and Bellitzer, on oxidative phosphorylation.

At the First Moscow Medical Institute, Baron was conducting interesting studies on serous membranes, innervation of arteries, and the development of Pacchionian granulations in dogs exposed to rapid rotatory motion.

Studies on immunity and electrophoretic effects of antibiotics on bacteria were being pursued at the Department of Biochemistry of Microbes and Immunity. Localization of points of origin of cardiac impulses on perfused human hearts and localization of damage to peripheral nerves by means of electroneurograms were problems being pursued at the Botkin Hospital. Shabad was resuming his work on the carcinogenic substances found in human tissues, and studies on the effect of tumors on cathepsins were under way.

GENERAL IMPRESSIONS OF MEDICAL RESEARCH IN THE SOVIET UNION

We received a favorable impression of medical research in the Soviet Union as it was being carried out in the few institutions visited by us during our month in Moscow at the height of the war. It is obvious that visits to eight research institutes, three hospitals, and one medical school, augmented by two major conferences and several minor ones, do not represent an adequate sample, and one month is not a sufficient length of time upon which to base any generalizations. We were, of course, shown the best places and met the outstanding workers, and were otherwise treated as guests. Although some extrapolation of our observations can be made, on the whole, any conclusions are limited by the extent of our actual observations. Moreover, the experiences are now two years old.

The Soviet medical authorities made every effort to provide us with personal, unsupervised contacts with their medical scientists and, in so far as they were able, to accede to our requests for specific information on matters pertaining to medical research. The approximately 100 scientists whom we had an opportunity to meet and with whom we discussed questions of medical research were friendly and frank in telling us of their work.

Medical research in the Soviet Union seemed to us to be in a healthy state, although it was carried out under difficulties resulting from the exigencies of war. We were told of experiments which had been unsuccessful as well as successful, of conclu-

sions which had been wrong as well as right, and the work of colleagues was occasionally questioned as well as praised. These experiences emphasize the fact that, at the working level, science and scientists are much the same in the Soviet Union as they are in the United States or elsewhere. Only with respect to facilities for work did there seem to be a difference.

The institutes which we visited were housed in quarters of variable quality. All of the laboratories had suffered from the privations and damage of war and the equipment was often inadequate compared with that of American laboratories. The hospitals were overcrowded, with stained though clean unbleached bed linen and gowns. These conditions were unavoidable, and allowance must be made for the circumstances. Surgical tables, lamps, and anesthesia equipment even in the best hospitals in Moscow were often antiquated by American standards.

Scientific monographs, textbooks, and journals were badly needed, although L. Bassias, director of the Central State Medical Library, had developed a splendid organization for distributing translations and abstracts to scientific members.

Although Soviet scientists told us in adequate detail of their work, we learned of no new practical research developments in medicine which we would regard as definitely superior to developments in the same field made by English, American, and Canadian scientists. Soviet scientists are progressing soundly along many lines also being developed by our investigators. Both they and we would profit by greater familiarity with the work going forward in both countries. The Soviet scientists and medical governmental authorities admire the work of our scientists, are most friendly toward them, and desire a closer cooperation among the workers of our countries. It is our conviction that increased interchange of scientific knowledge and personnel between the United States and the Soviet Union would be mutually stimulating and beneficial.

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Technical Papers

Acetylcholine Synthesis¹

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Acetylcholine participates in the humoral transmission of the effects of nervous stimulation in cholinergic systems. Acetylcholine is released during stimulation of the vagus, the motor nerves to skeletal muscle, the preganglionic fibers of the sympathetic nervous system, and perhaps when impulses cross the synapses of the spinal cord (1, 2, 4, 5, 10, 13). It is inferred that acetylcholine is synthesized in the central nervous system and probably also in peripheral nerve tissue, since the amount of acetylcholine liberated during prolonged stimulation may be several times the amount contained in nonstimulated nerve tissue (9). Nerve tissues synthesize acetylcholine even *in vitro*, and there is evidence that the synthesis of acetylcholine results from the activity of a specific enzyme (6-8, 11, 12, 14-16, 32). The amount of acetylcholine synthesized is probably regulated by the dynamic equilibrium of the various metabolites that surround the enzyme-substrate complex during the process of synthesis.

In the presence of blood serum and spinal fluid more acetylcholine is synthesized by nerve tissue *in vitro* than in the absence of serum and spinal fluid (16, 17). Some of the potentiator substances diffuse through Cellophane membrane (16). Although serum contains both potentiator and inhibitor substances, the potentiator effect prevails. The potentiator effect may be reduced by various physiological procedures, e.g. less acetylcholine is synthesized in the presence of serum collected from the fatigued arm than in the presence of serum collected from the resting arm (25). The effect of the serum and spinal fluid in increasing acetylcholine synthesis is reduced in patients with myasthenia gravis (16, 17).

To ascertain the nature of substances having the ability to modify synthesis of acetylcholine the effects of various known metabolites on acetylcholine synthesis *in vitro* were investigated.

Compounds containing energy-rich phosphate bonds (14, 30), some products of carbohydrate metabolism (21), lower fatty acids (28), polypeptides and amino acids (26) increase the amount of acetylcholine synthesized. Some decomposition products of nucleic

acid (23) and of organic phosphates occurring in the body (inosinic acid 23; ammonia 15, 26) decrease acetylcholine synthesis.

Of the inorganic ions potassium (12, 33), phosphate (15), rubidium (12), caesium (12), barium (31), magnesium (31), and manganese (31) increase the synthesis, whereas potassium in high concentrations (12), calcium (12, 14), and ammonia (15, 26) decrease it.

Hormones also exert an effect on acetylcholine synthesis. Ether extracts of thymus and pancreas decrease the synthesis (19), while similar ether extracts of other tissues tested (lymph gland, thyroid, salivary gland, lung, and subcutaneous fat) do not. Since the size of the thymus is regulated by the adrenotropic hormone of the pituitary gland, this hormone was administered to living animals, and the ability of brain to synthesize acetylcholine was ascertained (20). Brain from animals injected with the adrenotropic hormone synthesized more acetylcholine than brain of non-injected animals. Most steroid hormones decreased the amount of acetylcholine synthesized, but estrogenic hormones and Δ^5 pregnenolone increased the synthesis (22). Thyroxine increased the acetylcholine synthesis (26), as did epinephrine (18). The effect of epinephrine in increasing the amount of acetylcholine synthesized may explain why epinephrine increases the effect of acetylcholine in the central nervous system and improves transmission from nerve to the muscle (3).

Vitamins may modify the amount of acetylcholine synthesized. Vitamin E, even in very low concentrations, vitamin C, and most members of the B group increase the amount of acetylcholine synthesized. Vitamin A and K in all the concentrations used, thiamine chloride and vitamin D in higher concentrations decrease the synthesis (24).

The variety of the above-enumerated substances suggests that many operate not by a specific action on the enzyme involved in the synthesis of acetylcholine but nonspecifically through other cell processes. Final evaluation of the factors that specifically affect acetylcholine synthesis can be made only after the enzyme system is isolated in pure form.

It is inferred that the enzyme involved in the acetylcholine synthesis contains an active -SH group, since the process is inhibited by agents that decrease the activity of the -SH group (monoiodoacetate, 14, 30; alloxan, 23; unsaturated ketones, oxidizing agents, 27; penicillin, 27) and is increased by agents protecting the activity of the -SH group (glutathione, eys-

¹This study was aided by a grant from the John and Mary R. Markle Foundation.

teine, 26; antioxidants, 24; sodium pyrophosphate in low concentrations, 23). The synthesis can occur aerobically and anaerobically (in the presence of an excess of energy-rich phosphate bonds, e.g. adenosine-triphosphate, 14, 30). The amount of acetylcholine synthesized depends on temperature (14, 16) and pH (optimum at alkaline pH, 29). The enzyme is located intracellularly (8).

On the basis of the above data the following postulate is presented. Normally occurring constituents of cells and extracellular fluid (serum, spinal fluid) modify the amount of acetylcholine synthesized in the living organism. Further, there is a dynamic equilibrium between potentiator substances (organic phosphates, metabolites of carbohydrates and fats, amino acids, inorganic ions, hormones, vitamins) and inhibitor substances (unsaturated and higher fatty acids, aromatic and heterocyclic compounds, steroid substances, inorganic ions, some decomposition products of nucleoproteins and organic phosphates). During physiological activity the original dynamic equilibrium is disturbed, and new dynamic equilibria are established. Certain metabolites of muscle released during prolonged work decrease the synthesis of acetylcholine (23, 25, 26). The accumulation of such metabolites is important in the production of fatigue resulting from indirect stimulation and secondary to decreased acetylcholine synthesis.

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Granulocytopenia and Anemia in Rats Fed Diets of Low Casein Content¹

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Granulocytopenia, correctable by crystalline L. casein factor (L.C.F., "folie acid"), has been found to occur occasionally in rats fed highly purified diets (4) and regularly when sulfonamides are included in such diets (3, 4, 7). Anemia (or impairment in erythropoiesis following hemorrhage) correctable by L.C.F. also has been found in rats fed sulfonamide-containing diets (1, 3, 6). Recently we have noted granulocytopenia in rats fed highly purified diets deficient in riboflavin and also among pair-fed, riboflavin-supplemented controls (5). Further investigation of this influence of inanition on the production of granulocytopenia has revealed limitation of casein intake to be a highly significant factor.

Weanling albino rats (Osborne and Mendel) were fed one of several purified diets differing only with respect to casein content. Diet No. 1055 contained no casein or protein and consisted principally of Crisco salt mixture, and dextrose.² In the other diets casein (Labco) in varying amounts replaced equivalent weights of dextrose. Total white blood cell counts, polymorphonuclear granulocyte counts, and hematocrit determinations were made as previously described (6). For the purposes of this report, granulocytopenia was considered to be present when the polymorphonuclear granulocytes numbered 500 or less per cu. mm. Anemia was considered to be present when the hematocrit was less than 30 vol. per cent.

Of 89 rats fed the casein-free diet (No. 1055), 10

¹ Presented in part by one of us (A. K.) before the AAAS Vitamin Conference at Gibson Island, Maryland, July 1945.

² The casein-free diet No. 1055 consisted of anhydrous dextrose, 86.76 grams; Crisco, 8.0 grams; salt mixture No. 550³, 4.0 grams; ferric citrate, 1.16 grams; and copper sulfate · 5H₂O, 0.08 grams. Into this diet were incorporated 1 mg. of thiamine hydrochloride, 2 mg. of riboflavin, 1 mg. of pyridoxine hydrochloride, 4 mg. of calcium pantothenate, 1 mg. of niacin, 200 mg. of choline chloride, 0.001 mg. of biotin, and 0.4 mg. of 2-methyl-1,4-naphthoquinone. Twice weekly each rat received a supplement of 0.25 cc. of corn oil containing 2,000 units of vitamin A and 200 units of vitamin D (Natola) and once weekly 3 mg. of α -tocopherol in 0.03 cc. of ethyl laurate.

died within 19 days after starting the experimental diet. One or more blood counts were made between the nineteenth and twenty-eighth days on the surviving 79 rats. Granulocytopenia was noted in 75 rats and anemia in 68. The 4 rats without granulocytopenia and the 11 rats without anemia failed to sur-

TABLE 1
GRANULOCYTOPENIA AND ANEMIA IN RATS FED PROTEIN-FREE DIETS AND PREVENTION WITH CASEIN

Group*	Diet	No. of rats	No. of rats with granulocytopenia†	No. of rats with anemia‡
A	0 per cent casein	8	8	6§
B	0 per cent casein—20 γ L.C.F. daily†	8	8	7§
C	18 per cent casein—pair-fed with Group A ..	8	2	0
D	18 per cent casein	8	0	0

* The 4 groups were equal with respect to sex, litter, and weight distribution. Food intake was ad libitum in groups A, B, and D.

† This crystalline fermentation product (2) was administered by pipette to each rat from the outset of the experiment.

‡ Noted within 28 days.

§ The rats which failed to develop anemia died after 19 to 25 days.

vive 28 days on the experimental diet. The average body weight was 42.5 grams at the start of the experiment and 30.2 grams after 20 days on the diet. Of 6 and 7 rats fed diets containing 2 and 4 per cent casein, respectively, all developed granulocytopenia within 30 days. Anemia was noted only among the rats fed the 2-per cent casein-containing diet. Seven of 8 rats fed an 8-per cent casein-containing diet developed granulocytopenia within 45 days; none had anemia.

Data on the influence of restriction of food intake and the effect of L.C.F. (2)³ administered preventively are in Table 1. These data indicate no significant preventive action by L.C.F. Severe restriction of an 18-per cent casein-containing diet (Group C) failed to produce blood dyscrasias in 6 of 8 rats. The 2 cases of granulocytopenia noted in this group may have resulted from inadequate casein intake.

Several materials were tested for their effectiveness in correction of granulocytopenia developed in rats fed the casein-free diet No. 1055. Treatment was administered daily for 4 days. A recount was made on the day following the last treatment. For the purposes of this report, a response was considered "positive" when the granulocytes numbered 1,000 or more cells per cu. mm. Further details and results of

³ The crystalline fermentation L.C.F. (2), synthetic L.C.F., and L.C.F. concentrate from liver used in these studies were furnished through the courtesy of Drs. E. L. R. Stokstad and B. L. Hutchlings, of Lederle Laboratories, Inc.

treatment are in Table 2. Rats which failed to survive the treatment period are not considered. When no treatment was administered, there was a progressive decline in granulocyte count and hematocrit value terminating in death. Of 13 rats treated with crystalline L.C.F. or a liver concentrate of L.C.F., only

TABLE 2
TREATMENT OF GRANULOCYTOPENIA

Treatment	No. of rats	No. of rats with positive response	Poly. granulocytes per cu. mm. (average)	
			Before treatment	After treatment
L.C.F.*—100 γ	8	2	350	750
L.C.F.†—200 γ subcutaneously	2	0	300	750
L.C.F.†—100 γ + L.C.F. conc.‡	3	0	33	417
—50 γ	9	0	217	39
Casein diets—18 per cent or 30 per cent	3	3	83	4,833
L.C.F.†—100 γ + L.C.F. conc.‡	5	5	350	3,090
—50 γ + casein diet—18 per cent	6	6	317	2,433

* Crystalline fermentation L.C.F. (2) or synthetic L.C.F. (Stokstad). No differences were observed between the activity of the two substances in these experiments.

† Crystalline fermentation L.C.F. (2).

‡ Contained in 0.058 grams of liver concentrate.

§ Synthetic L.C.F. (Stokstad).

2 reached granulocyte levels of 1,000 cells per cu. mm. Granulocyte values declined in all of 9 rats fed diets containing casein at levels of 18 or 30 per cent⁴ in place of the casein-free diet No. 1055. However, the administration of L.C.F. combined with a change to an 18-per cent casein-containing diet resulted in significant increases in granulocyte count in each of 8 rats. Similarly treatments with L.C.F. combined with the dietary administration of a mixture of purified amino acids⁵ produced significant increases in granulocyte count in each of 6 rats. Data on the treatment of anemia are incomplete and therefore are not presented at this time.

Further study is required to determine the identity of the amino acids responsible for the granulocytopoietic activity found in casein or in a mixture of purified amino acids. Such data may help in the elucidation of the mechanism of action of *L. casei* factor and the amino acids in the formation of granulocytes.

⁴ Five and 4 rats were fed diets containing 18 per cent and 30 per cent casein, respectively. Average daily intake of these diets per rat was 3.6 grams.

⁵ To mixture XII-c of W. C. Rose and S. S. Fierke (*J. biol. Chem.*, 1942, 143, 115) containing 18 amino acids were added 7.8 grams of dl threonine and 7.8 grams of dl aspartic acid. Of this final mixture, 26.7 grams (representing 18.0 grams of "active" amino acids) replaced an equal weight of dextrose in the casein-free diet No. 1055. Average daily intake of this diet per rat was 2.7 grams.

SUMMARY

Severe granulocytopenia and anemia were developed uniformly in rats fed protein-free diets. Casein (18 per cent) prevented these dyscrasias, but crystalline *L. casei* factor ("folic acid") did not prevent them. In the correction of granulocytopenia in rats fed protein-free diets, *L. casei* factor alone was only slightly effective, diets of higher casein content (18 or 30 per cent) were ineffective under the experimental conditions described. However, *L. casei* factor combined with an 18-per cent casein-containing diet or *L. casei* factor combined with a mixture of purified amino acids were found to be highly effective in correcting the granulocytopenia.

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The Presence and Significance of a Leukopenic Factor in Inflammatory Exudates

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A number of inflammatory conditions are accompanied by a fall in the number of circulating white blood cells, a so-called state of leukopenia. Fitz-Hugh and Krumbhaar (1) regard agranulocytosis as the result of an arrested development of leukocytic elements. The disease involves lymphoid elements as well as granulocytes. These authors therefore speak of the condition as a pernicious leukopenia. A profound leukopenia referable to a virus infection has been recently described to occur in cats (2, 3). It is interesting to note on close scrutiny the frequent occurrence of some infection accompanying an agranulocytic process.

The writer has demonstrated the presence of an injury factor located in, or at least closely associated with, the euglobulin fraction of inflammatory exudates (5). This substance has been termed necrosin. Recent studies indicate its more frequent recovery in exudates from a severe area of inflammation in which there is usually an appreciable degree of acidity (7). The whole euglobulin fraction of exudates not only induces marked cutaneous injury, but likewise it

causes in dogs a marked degree of fever and a profound leukopenia (5, 6). Subsequent investigation have revealed that the pyrogenic property of the whole euglobulin fraction of exudates is really not referable to necrosin, but that this fever-inducing capacity is caused by a completely different, but closely associated substance, termed by the writer pyrexin (6). The present preliminary communication indicates that in inflammatory exudates there exists a leukopenic factor which is not one of the biological attributes of necrosin *per se*. It is closely associated with pyrexin. Yet, it can readily be dissociated, at least to a large extent, from this pyrogenic factor. The presence of such a leukopenic factor in inflammatory exudates may in large part explain, perhaps, the state of leukopenia accompanying numerous inflammatory processes. The leukocytosis-promoting factor present in exudates may well mask the ultimate effect of the leukopenic factor (4). In brief, the final blood picture accompanying an acute inflammatory process may to a large extent depend on the relative concentration of either the leukocytosis-promoting factor (LPF) or the leukopenic factor now under discussion, both of which factors are produced at the site of an acute inflammation.

An inflammatory exudate at an acid pH will, when injected into the circulation of a dog, tend to induce a rapid and sharp fall in the number of circulating leukocytes. This is a conspicuous feature within the first hour or so. The average fall in 8 experiments has been found to be 3,778 white blood cells per cubic millimeter or 32.3 per cent. Pyrexin, as isolated from such exudates, is the fraction obtained which has been found to induce a marked leukopenia. The average fall in 10 experiments is 9,980 white blood cells per cubic millimeter, a drop of 79 per cent. It is possible that the simultaneous presence of the LPF in the whole exudate counteracts somewhat the full effectiveness of the leukopenic factor. Such a state of affairs would account for the more striking effect obtained with pyrexin where the LPF is absent. Purified necrosin or normal blood serum utterly fails to induce any such drop in the leukocyte count. Within the usual period of study (about 6 hours) the maximum decrease in the number of circulating leukocytes is under normal circumstances, negligible.

An attempt has been made to dissociate the leukopenic factor from pyrexin. Some recent evidence indicates that the latter is, or is at least associated with, a polypeptide. It is possible that the leukopenic factor also belongs to this group, especially since it is derived from pyrexin. For this reason pyrexin has been partially hydrolyzed with 0.1 N HCl for about 10 to 15 minutes in an effort to determine

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whether pyrexin can be in large part inactivated, while leaving behind an active leukopenic factor. The scheme of extraction adopted follows:

SCHEME OF EXTRACTION OF LEUKOPENIC FACTOR

Exudate
 $(\text{NH}_4)_2\text{SO}_4$ at 1/3 saturation
 precipitate
 treated with distilled water
 shake
 insoluble material
 dialyze until free of SO_4
 pyrexin (dried by freezing)
 reflux with 0.1 N HCl for 10-15 minutes
 cool
 N NaOH adjusted to pH 10 or 10.3
 concentrate on steam bath to about 1/10th volume
 dialyze
 evaporate to dryness on steam bath or dry freeze
 (leukopenic factor)

The final material obtained when extracted from pyrexin, as indicated above, still induces a marked leukopenia. This, as in the case of the whole exudate, develops abruptly, and it may last a few hours. The average fall in 14 experiments is 6,146 cells per cubic millimeter, a drop of over 50 per cent. Yet, this leukopenic factor is now essentially dissociated from pyrexin, for it essentially causes no fever when injected into the blood stream of dogs. Preliminary observations in collaboration with Dr. Frederick Bernheim, to be subsequently reported in detail, on the amino nitrogen concentration before and after hydrolysis indicate that the leukopenic factor seems to belong to the group of polypeptides. It is thermostable, for boiling fails to inactivate its effect. Various controls, such, for instance, as the normal variation in leukocyte counts and in temperature level during the period of study (i.e. within about 6 hours) or the reagents themselves that were utilized in dissociating the leukopenic factor from pyrexin, all indicate that the effect of the leukopenic factor is indeed real. These studies are being pursued further and will be reported *in extenso* elsewhere.

In brief, evidence has been advanced to indicate that there exists in inflammatory exudates, particularly when obtained from an area of severe inflammation and therefore usually at an acid pH, a leukopenic factor, which *per se* may offer a reasonable explanation for the development of a state of leukopenia with some of the types of acute inflammation. Furthermore, in the exudative material this leuko-

penic factor seems to be in close association with pyrexin, the pyrogenic factor from which in turn it can to a large extent be separated. The leukopenic factor affects the granulocytes as well as the mononuclear cells, for the latter are likewise depressed. The effect is a general one. The leukopenia is found to exist both in the peripheral circulation and in samples of blood obtained from the heart.

In subsequent studies since this communication was sent for publication, it has been found that, although the leukopenic factor of inflammatory exudate is mostly found in close association with pyrexin, it can be recovered sometimes to some extent in other fractions of exudative material, indicating that it is apparently not exclusively found in association with pyrexin. Furthermore, additional studies seem to indicate that the leukopenic factor of exudates does not primarily deplete the bone marrow, but rather the mechanism involved appears to be a rapid trapping of leukocytes in the alveolar walls of the lungs, in the sinusoids of the liver, and apparently in the spleen. The latter fact may be of significance in our further understanding of the mechanism involved in the acute splenic tumor accompanying numerous inflammatory processes.

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The Comparative Toxicity of Thiourea to Four Mutants of *Drosophila melanogaster*¹

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 Washington Square College of Arts and Science,
 New York University

During the course of an investigation of the effects of a number of drugs upon the development of several genotypes of *Drosophila melanogaster*, the striking toxicity of thiourea² was observed. A survey of the literature disclosed several reports dealing with thiourea as an insecticide. Two-per cent solutions of thiourea and phenylthiourea were effective against the webbing clothes moth (9). Third instar blowfly larvae died in the third or fourth instar when exposed to thiourea incorporated in their food (6). McGovran, Richardson and Piquett (8) observed a 92-per cent

¹ Acknowledgment is made to Miss Ada Rakos for technical assistance.

² The authors are indebted to Dr. Stanton M. Hardy, of the Lederle Laboratories for a supply of thiourea.

mortality in the housefly (*Musca domestica*) when third instar larvae were raised on a medium containing 7.5 mg. of thiourea per 23 grams of food. Sixty milligrams of borax were needed to produce the same mortality, and this amount of DDT yielded a death rate of 88 per cent. In another investigation DDT was found to be more effective than a 1-per cent solution of thiourea in reducing the number of emerging flies (11). Feeding a mixture containing 10 per cent of allyl thiourea and 90 per cent kaolin to third instar larvae of the silkworm, *Bombyx mori*, produced no unfavorable effects (1).

The following is offered as controlled, quantitative evidence of the effectiveness of thiourea in destroying larval diptera.

EXPERIMENTAL METHOD

Pearl's (10) synthetic medium, S-101, modified by changing the agar content from 2.2 to 2.5 per cent, served as the basic food. To this medium thiourea was added to give the desired concentrations (Table 1). The food was poured into 1 x 4-inch vials to a depth of $\frac{1}{8}$ inch and was yeasted when cool (one drop of a yeast suspension of one cake of Fleischman's yeast per 100 cc. of water was placed on the surface of the food). The cultures were allowed to stand for 24 hours for yeast growth.

TABLE 1
EFFECT OF THIOUREA ON MORTALITY OF *D. melanogaster*

Conc. of thiourea Mg./100 cc. of food	Ebony		Sooty		Black		Wild-type	
	No. of larvae	Mortality %						
12.5	200	100			210	100		
10.0	200	100	200	100	210	100		
8.0	400	97	200	98	400	84	360	75
7.5	210	96			210	85		
7.0	400	98	200	83	400	76	385	72
6.0	400	87	200	84	360	65	360	59
5.0	370	75	200	66	440	58		

Ten newly-hatched larvae were placed in each vial and incubated at $25^\circ \pm 0.05^\circ$ C. The four genotypes, ebony, sooty, black, and Wild-type, were tested in these experiments. The animals were examined at intervals during the larval and subsequent developmental periods.

A number of preliminary runs established that at concentrations ranging from 250 mg. to 20 mg. of thiourea/100 cc. of food all larvae died in the first or second instar. This obtained for dosages of 12.5 and 10 mg./100 cc. of food, with a rare individual reaching the third instar and attempting puparium formation. In the final experiments concentrations ranging from 12.5 to 5 mg./100 cc. were used.

RESULTS AND DISCUSSION

Genetic considerations. The data indicate a marked genetic difference in the resistance of these four stocks to the drug, the Wild-type being the most resistant of the four genotypes tested. Black is a II-chromosome recessive mutant, and ebony¹¹ a III-chromosome recessive mutant from the Wild-type. These two mutants are phenotypically indistinguishable and have normal viability on standard culture media. However, they show a marked difference in resistance to thiourea, black being much more so than ebony. The recessive mutant, sooty, is an allele of ebony and only a slight departure from the Wild-type body color as compared to the black color of the ebony¹¹ flies. The sooty genotype seems to withstand the drug better than its allele, ebony. This difference may be more marked than the data appear to indicate. The black and ebony¹¹ stocks were single locus differences from the Wild-type stock, but the sooty stock also carried the mutants, curled wing, stripe, scarlet, peach, rough-hairy, and thread—a total of eight mutant loci differences from the Wild-type stock. The cumulative deleterious effects of mutants in compound stocks is well known. It may be that the rather close approach of the sooty mortality to that of its allele, ebony (Table 1), is due in large part to this cumulative effect. If this is so, then the true mortality of the sooty allele is much lower than the figure indicated. This would bring its resistance to the drug more nearly into line with its slight deviation from the Wild-type body color, making the sooty gene both physiologically and morphologically a less extreme variation than the ebony gene from their Wild-type allele. The marked mortality difference between the phenotypically similar black and ebony stocks shows that there must be significant differences in the nonvisible physiological effects of the genes at these two loci. We have observed marked developmental-morphological effects of thiourea at certain dosages. These results are being reported elsewhere. One of us has found different developmental effects of other unrelated drugs on *D. melanogaster* (Harnly, in press). It is evident that the use of drugs might prove a profitable technique in the study of the nature of gene action with *D. melanogaster*.

Thiourea as a larvicide. The numbers of individuals treated and the mortalities of the four genotypes at the indicated dosages are given in Table 1. The mortality values are calculated on the number of emerged adult flies. Examination of the table reveals that a concentration of 12.5 and 10 mg./100 cc. produced 100-per cent mortality in the mutants, ebony, sooty, and black. The trend of the data indicates that a 100-per cent mortality of the wild-type would be produced at some concentration between 15 and 16

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mg./100 cc. At lower concentrations of 8-5 mg./100 cc. there was a progressive decrease in the death rate. It is evident that even in concentrations as low as 0.005 per cent thiourea is highly toxic to *D. melanogaster*.

Following recent large-scale field spraying of DDT to destroy mosquitoes, wholesale destruction of fish and other fresh-water life was observed. It should be noted that thiourea has no such lethal action upon fish and amphibia. Immersion of young individuals of *Xiphophorus hellerii* and *Platypoecilus maculatus* in water containing 33.3 mg. of thiourea/100 cc. for periods up to five months resulted in vigorous fish which did, however, exhibit retarded growth and development (3). It has been demonstrated that animals (frogs, 4, 5, 7; and mammals, 2) retarded by thiourea will resume normal growth and development upon discontinuation of the thiourea treatment. It should be emphasized further that the nonlethal concentration employed in the fish experiment is more

than 300 per cent higher than that which yielded 100-per cent mortality in *Drosophila* larvae.

In view of these facts it was considered worth while to investigate the effects of thiourea upon mosquito larvae. The results of these tests will appear in a subsequent publication.

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News and Notes

Ray G. Daggs has been appointed director of research at the Armored Medical Research Laboratory, Fort Knox, Kentucky.

Jean Brachet, of the University of Brussels, has been appointed visiting professor of zoology at the University of Pennsylvania for the period January to September 1947. He will teach and conduct research in experimental and chemical embryology at the University during the spring term and work at the Marine Biological Laboratory, Woods Hole, during the summer. Thus, graduate students may work continuously with Dr. Brachet during the entire period.

Ernest Laqueur, Institute of Pharmacotherapy, Amsterdam, delivered the Seventh Harvey Lecture of the current series at the New York Academy of Medicine on 18 April 1946. Dr. Laqueur spoke on: "Interrelationships Between Gonadotropic and Sex Hormones."

R. R. McGregor, senior fellow, Mellon Institute of Science Teachers Association on 1 May 1946. Dr. McGregor, Industrial Research, Pittsburgh, addressed a joint meeting of the Franklin Institute and the Philadelphia Gregor spoke on "Silicones: Food for Imagination."

Lee A. DuBridge, who returned to the Department of Physics at the University of Rochester in February from the NDRC Radiation Laboratory, Cambridge, has been made president of California Institute of Technology. He succeeds Dr. R. A. Millikan, who retires this spring.

T. Wayland Vaughan, of Washington, D. C., former director of the Scripps Institution of Oceanography, has been awarded the Mary Clark Thompson medal by the National Academy of Sciences. Dr. Vaughan was honored by this award "in recognition of his outstanding achievement in such purposeful and ingenious coordination of observations and generalizations made in and bearing on the fields of stratigraphic geology and paleontology."

Charles B. Fawcett, geographer of the University of London, will be in residence at the Clark University School of Geography during the second semester, February to May 1947. He will offer regular courses of instruction and a series of special lectures during his stay in the United States.

Arthur L. Samuel, of Bell Telephone Laboratories, New York, will become a member of the electrical engineering faculty at the University of Illinois.

Announcements

Frédéric Bremer, of the University of Brussels, has written that the ship carrying the American scientific periodicals which appeared during the war struck a mine, and that the 1946 periodicals have not been received regularly. He would appreciate receipt of reprints from his American colleagues, especially on the subjects of neurophysiology, physiology of the muscle, and physiology of the circulatory system. These papers will be of great value to Prof. Bremer, as he has been asked to write an article on the general physiology of the nerve centers for the *Annual Review of Physiology*, 1947 (covering works appearing in 1945-1946).

Prof. Bremer's address is: Faculté de Médecine et de Pharmacie, Université de Bruxelles, 115 Boulevard de Waterloo, Bruxelles.

The Department of Animal Husbandry, Pennsylvania State College, is the recipient of a research grant from Sharp and Dohme. This grant is a renewal of previous grants and affords increased financial support to a research program under the direction of W. T. S. Thorp, professor of animal pathology. Dr. Thorp is making an extensive study of various sulfonamides in the treatment of infectious and parasitic diseases in livestock and poultry.

The Committee on Growth of the National Research Council, acting for the American Cancer Society, announces that it will entertain applications for grants in cancer research to become effective 1 July 1947. Applications will be received until 15 September 1946.

Applications for fellowships and senior fellowships in cancer research of the American Cancer Society for the ensuing year will be received until 1 December 1946.

To date the Committee on Growth has recommended to the American Cancer Society a total of 75 research grants and 14 fellowships. The Committee will continue to recommend support of research in the basic sciences and in clinical investigative medicine broadly pertaining to problems of growth. It will continue also to rely heavily for counsel on its advisory Divisions of Chemistry, Biology, Physics, and Clinical Investigations and their subjacent panels in specialized areas of research.

Applications for research grants for the current year will no longer be entertained. Communications should be addressed to: The Committee on Growth, Division of Medical Sciences, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

Rohrer, Hibler & Replogle announce the opening of another regional office which is located in Suite

520, Terminal Tower, Cleveland, Ohio. J. Elliott Janney is resident partner in charge.

Five fellowships have been established by the New York State Department of Health for the training of physicians in the public health laboratory field. The appointments are for a period of one year and are open to physicians with postgraduate laboratory training who wish additional experience in pathology, bacteriology, or biochemistry to qualify for positions in the public health laboratories in New York. Candidates must be United States citizens who have graduated from a medical school approved by the American Medical Association and who are licensed or eligible to take the examination for license to practice medicine in New York State. Inquiries should be directed to the Division of Laboratories and Research, State Department of Health, Albany 1, New York.

Karl Sandved, Norges Tekniske Høgskule, Trondheim, Norway, has written:

As I suppose you can imagine only too well, confinement and prison are not likely to give increased stimulus to scientific research. It was a great event for me and some five other countrymen, therefore, to receive an invitation to England by the British Council. I am just back in Trondheim again after three very interesting and busy weeks in England.

We have had, and still have, certain difficulties in our daily work in the Chemistry Department. Dr. Sørensen is the only one of our prewar professors back in office at the present moment. He had one kidney removed during the war, due to a Gestapo bullet fired through his back, when he was in for a third-degree cross-examination. Prof. Tronstad was killed up in the mountains, Prof. Rader is in the hospital, and Prof. Schmidt-Nielsen has retired. I was lucky enough, on my own part, to keep out of the reach of the Gestapo. Still we have had many encouragements, not least from across the Atlantic.—*Victor K. LaMer* (Columbia University).

Philips Technical Review, which was published monthly before the war in four languages by the Research Laboratory of N. V. Philips Gloeilampenfabrieken, Eindhoven, Holland, has resumed publication, according to an announcement by O. S. Duffendack, president of Philips Laboratories, Inc.

Dr. Duffendack explained that publication of international editions of the *Review* was forbidden by the Nazis at the beginning of 1942, although the Dutch edition was permitted to continue until July. The seventh volume, 1942, therefore consisted of only six numbers. It is planned to make these available in the English edition as soon as possible.

First issues of Vol. 8, No. 1, of the English edition, just received in this country, contain papers on: "Sintered glass," by E. G. Dorgelo; "An X-ray ap-

paratus for contact therapy," by H. A. G. Hazeu, J. M. Ledebot, and J. H. van der Tuuk; "The measurement of impedances particularly on decimetre waves," by J. M. van Hofweegen; and "An apparatus for stroboscopic observation," by S. L. de Bruin.

Subscriptions for the *Review* are being handled exclusively in this country by Elsevier Publishing Company, 215 Fourth Avenue, New York. Yearly subscription price for 12 monthly issues is \$5.00 including postage.

A letter addressed to Prof. Frédéric Roman, successor of the late Charles Depéret as professor of geology, University of Lyon, France, was recently returned, marked "Décédé." Roman was a specialist on Cenozoic stratigraphy and mammalian paleontology.—*Horace E. Wood, II* (University of Newark).

The Department of Electrical Engineering of the Illinois Institute of Technology has announced that the Graduate Fellowship in Power Systems Engineering, which the Westinghouse Educational Foundation first established at Illinois Tech in 1945, has been re-established on a yearly basis for a period of five years, according to Louis T. Radar, chairman. Applications for this year's fellowship are being accepted by Dr. Radar and must be received by him before 1 June 1946. The final decision will be announced to all applicants by 16 June. The appointment will become effective 23 September.

One fellow will be selected each year by a joint committee representing both the Foundation and the Institute. Leading to a degree of Master of Science in Electrical Engineering, this fellowship provides a stipend of \$1,500 with all tuition fees paid for 12 months.

Meetings

The American Geophysical Union will hold its 27th annual meeting 27-29 May in the Hall of Government, George Washington University, Washington, D. C. The general meetings of the Union will consist of: an evening lecture session on the volcano, Paricutin; a business session; and an informal smoker at the Cosmos Club. In addition to business meetings, 123 papers have been scheduled for presentation in the sections on geodesy, seismology, meteorology, terrestrial magnetism and electricity, oceanography, volcanology, hydrology, and tectonophysics.

The eighth summer conference of the New England Association of Chemistry Teachers will be held 19-24 August at Middlebury College, Middlebury, Vermont. The summer conference has become an event of increasing professional importance among college and secondary school chemistry instructors.

Two symposia are to be held. A symposium on "Electrolysis" will be presented by William B. Meldrum, Haverford College; Frank T. Gucker, Northwestern University; and John A. Timm, Simmons College. A symposium on "Colloids" will be headed by Ernst A. Hauser, Massachusetts Institute of Technology, accompanied by other well-known authorities.

Other program features include: "Silicones," by Francis J. Norton, General Electric Research Laboratories, Schenectady, New York; "Chemistry in Life Insurance," by Sidney H. Roberts, Aetna Life Insurance Company Medical Laboratory, Hartford, Connecticut; "A GI Chemist in a GI School in France," by Andrew J. Scarlett, Dartmouth College; and other papers to be announced.

Elections

The Kappa Chapter of Sigma Xi at Columbia University held its annual initiation ceremony and banquet, on the evening of 7 May, at which 53 members-elect were initiated. Officers elected for 1946 are: Walter Rautenstrauch, president; I. I. Rabi, vice-president; and John S. Karling, secretary-treasurer. Following the banquet, Edward U. Condon, director of the National Bureau of Standards, addressed the meeting on "The Liberation of Atomic Energy."

The American Society of Naturalists has elected the following officers for the year 1946: C. W. Metz, University of Pennsylvania, president; H. A. Spoehr, Carnegie Institution of Washington and Stanford University, vice-president. William R. Taylor, University of Michigan, continues as secretary, and T. M. Sonnenborn, Indiana University, as treasurer.

The Utah State Chapter of the Society of the Sigma Xi held its annual business meeting on 8 April 1946. Officers elected at the meeting include: Datus M. Hammond, president; George T. Blanch, vice-president; and Carroll I. Draper, treasurer. The retiring president, J. Stewart Williams, is retained on the Executive Committee with the secretary, Marion T. Bird, who has completed the first year of a three-year term.

The Society of Neurological Surgeons elected as its new president, W. M. Craig, of the Mayo Clinic, Rochester, New York, at a meeting at Vanderbilt University, Nashville, Tennessee, on 9 April.

Recent Deaths

William E. Evans, Jr., 40, associate professor of pharmacology, University of Maryland School of Medicine, died in the University Hospital on 6 May after an illness of short duration.

Letters to the Editor

The Effect of DDT on Cutaneous Sensations in Man

A group of 32 students of Yenching University volunteered for a study of the effect of DDT on cutaneous sensations in the skin when kept in constant contact with this agent. Each student wore a piece of cheesecloth (3 x 4 cm.) saturated with a solution of DDT or mixture of this agent, on the inner surface of one forearm and another piece containing only the diluent on the other arm as a control. The cloths were put on corresponding areas on both sides, 6 cm. above the lowest transverse furrow of the wrist. Cutaneous sensations of the covered areas have been followed through a period of five weeks. The tactile sensation was tested by calibrated Von Frey's hairs, and the pain, cold, and heat sensations by spot distribution.

Students were divided into groups of four or five each, and each group was dressed with a different concentration or mixture of DDT. While no remarkable difference in pain, cold, and heat sensations could be detected, the solution of DDT in olive oil or mixture with vaseline (petrolatum) has been found to desensitize the tactile sensation in most cases, as shown in Table 1. The minimal pressure that would arouse the tactile sensation of the skin in contact with the olive oil solution or vase-

TABLE 1

Diluent	% DDT	No. of cases showing desensitized tactile sensation	No. of cases showing sensitized tactile sensation	No. of cases showing no effect
Olive oil	20	3	0	1
Olive oil	10	3	0	1
Olive oil	5	2	1	1
Vaseline (petrolatum)	20	3	0	0
"	10	3	0	1
"	5	0	0	4
Talc powder ...	10	1	0	4
None	100	0	0	4

line mixture of DDT was 1-2.5 grams per square centimeter higher than the control. These results indicate that oil facilitates the penetration of DDT into the skin.

YIN-CH'ANG CHIN and CHI-HSUEH T'ANT

Department of Biology, Yenching University
Chengtu, China

Arginine-free Diets and Intestinal Synthesis of Arginine

The white rat is able to synthesize sufficient arginine for moderate growth, reproduction, and partial lactation (H. L. Williams and E. M. Watson, *Rev. Canad. Biol.*, 1944, 3, 426). The possibility that arginine is one of the amino acids which C. J. Martin (*Proc. Soc. exp. Biol. Med.*, 1944, 55, 182) believes to be synthesized within the intestinal tract led to the following investigation.

The stock diet of the colony of albino rats was Fox

Chow. The arginine-free diet was prepared as reported earlier by Williams and Watson and, when modified by the addition of 2 per cent sulfasuxidine, was supplemented with 2-me-1,4-naphthoquinone (50 mg./kg. diet), biotin concentrate (200 µg. No. 1,000/kg.), but not with folie acid as employed by Martin.

Because of the lack of available chemicals, this series was restricted to three animals on each of the arginine-free diets. The average weights of these animals while on the test diets are shown in Table 1.

TABLE 1
EFFECT OF ARGinine-FREE DIETS ON WEIGHTS OF MALE WHITE RATS

Weeks	Arginine-free diet	Arginine-free diet + sulfasuxidine
	grams	grams
1	151	145
2	147	138
3	147	138
4	149	137
5	150	138
6	152	142
7	157	140
8	162	145
9	152	138
	145	126

Although the rats failed to gain weight on either diet, possibly due to the restricted intake, there was no indication of the dramatic loss of weight known to accompany acute amino-acid deficiency either by the group or by individual animals. None of the animals died. Weights, dry weights, and arginine content of the various organs from animals of both series obtained at autopsy compared favorably with comparable data from control animals of the same age fed Fox Chow, in confirmation of findings of Williams and Watson. Thus it is suggested that the intestinal tract is not the source of the arginine synthesized by the rat.

This work was supported by a research fellowship in nutrition from Swift Canadian Company, Ltd.

H. L. WILLIAMS and E. M. WATSON

The Meek Memorial Laboratory
University of Western Ontario Medical School

The Successful Transfer of Ovaries Between Dogs of Different Breed

For a number of years, experiments have been in progress in an endeavor to transplant ovaries between dogs of different breed. The object of the present note is to report two successful transfers of this type and to record preliminary observations on the behavior of the recipient animals. Early unsuccessful experiments were carried out without regard to the physiological status of the dogs, and the present successful transfers appear to be directly related to the use of recipients in oestrus.

The operative procedure employed is extremely simple. After incising the capsule, the ovary is removed at the

hilus. The donor's ovary is secured in position in the capsule of the recipient with several fine catgut sutures and the capsule closed. Ovariectomy and transfer are performed on both sides at the same operation.

In both of the successful transfers the donors were bloodhounds and the recipients foxhounds. The bloodhounds were eight years old and had passed the period of productive breeding. The foxhounds were young animals, and each had whelped and raised one litter previous to transfer. Both were in oestrus at the time of operation.

Following transfer, signs of oestrus decreased gradually over a period of four or five days but then recurred in full intensity and continued for a normal cycle of 20 days. Both dogs copulated during this period, but neither conceived. The dogs were followed carefully thereafter, and it was with considerable surprise that signs of a second oestrus were observed 49 days after the start of the previous period in one animal and on the 98th day in the other. It appears significant that such periods of heat do not correspond with the recipient's previous history, but on the contrary, represent a continuation of the bloodhound donor's cycles.

One of the dogs was killed for study 70 days after termination of the second oestrus. The ovaries appeared normal on gross examination, and histological section showed corpora lutea and innumerable follicles in various stages of maturation. An estimation of the number of follicles was not attempted, but it was at once apparent that they greatly exceeded the quantity normally found in the ovary of an eight-year-old dog. The hilus was of interest particularly in its content of blood vessels. Some of them were normal in appearance, filled with blood cells, and undoubtedly represented vascularization of the transplant by the new host. Others were necrotic or showed the extensive hyalinization characteristic of the senile ovary.

The behavior of the animals after operation as well as the morphology of the transplanted organs attest the successful transfer of ovaries between dogs of different breed. It is significant that each of the successful transfers was effected during the recipient's oestrus and that numerous experiments performed on other periods of the sexual cycle terminated in failure. The continuation of the donor's cycle after transfer was contrary to expectation and suggests that the initiation of oestrus is a function of the ovary rather than of the pituitary. These studies are being continued and will be reported in more detail in a later publication.

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**Work of the International Commission
on Zoological Nomenclature**

Throughout the war and since, the International Commission on Zoological Nomenclature has received much practical help and encouragement from American zoological institutions and from individual American zoologists. This has greatly contributed to the success of the efforts of the Commission to develop its work and thereby raise

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the standard of service rendered to the zoological profession. In spite of wartime difficulties the Commission was able between 1942 and the end of 1945 to issue between 70 and 80 separate publications on various questions of zoological nomenclature. The extremely scanty funds at its disposal made it inevitable that the Commission should charge a relatively high price for the publications so issued. The Commission has always regretted that this should have been necessary, since it holds the view that fundamental publications of this kind should be issued at prices sufficiently low as to be within the financial means of all interested workers. It has therefore always set itself the aim of reducing the prices charged for its publications as soon as its financial resources rendered this practicable.

The Commission has recently reviewed the general position in the light of the encouraging financial results obtained in the year 1945 (full particulars of which, together with the accounts for 1945, will shortly be published by the Commission in its *Bulletin of Zoological Nomenclature*). As the result of this survey, the Commission has decided to cut by 30 per cent the scale of charges for all publications issued after 1 February 1946. This decision involves a considerable financial risk to the Commission. However, it is a wise decision and one which will be widely welcomed by zoologists generally. It is a matter of particular interest to American zoologists, some of whom have been urging the Commission for some time to take action on these lines.

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Scientific Independence in Russia

In his reply to Dr. Asmous on Russia, Mr. Gaposchkin (*Science*, 1946, 103, 404) appears to evade all of the issues completely. He starts out by saying that it is surprising that in 1946 a letter such as that of Dr. Asmous could appear in a scientific periodical. To support that thesis he suggests that Dr. Asmous' life and the lives of all other Americans have been saved by Russia. That statement, even if it were true, would be quite beside the point. Dr. Asmous, in his letter, repeated the charge already made by K. Sax that "science (in the USSR) must conform to political philosophy." Mr. Gaposchkin says not a word in answer to that charge. He remains silent regarding the question of the circumstances surrounding the death of N. Vavilov, a question which has for some time caused, and continues to cause, much mental distress among the latter's scientific colleagues in all parts of the world. While the case of N. Vavilov is a single instance, does it not constitute a symptom of a serious disorder? Can scientists, or indeed any other citizens of democracies, afford to overlook that symptom or the ailment to which it points? Is it too much to expect of those who wish to hold a brief for the independence of science and scientists in the USSR that they either satisfy their colleagues that such charges are unfounded or that the basis for them has ceased to exist?

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Book Reviews

Essentials of general chemistry. B. Smith Hopkins and John C. Bailar, Jr. Boston: D. C. Heath, 1946. Pp. v + 520. (Illustrated.) \$3.50.

In the freshman course in general chemistry the teacher must attempt to accomplish much more than to start the training of specialists. In addition to future chemists, those enrolled in the course will include both students who have studied chemistry in high school and those who have not; students preparing for such diverse professional fields as engineering, medicine, nursing, home economics, and agriculture; and students for whom the beginning course in chemistry will be their only contact with scientific thought in their entire college program. Enrollment in the general chemistry course may be as large as 3,000 in many of the state universities, and the teacher may be required to pass all but a small percentage of these. The writing of a successful textbook for such an audience requires great skill and experience, and it is to the credit of the authors that they have succeeded so well.

By the inclusion of a greater amount of descriptive chemistry than is usual for textbooks at this level they attempt to make up for the deficiencies of students with poor preparation; and by the skillful introduction of modern theory and using it to explain and correlate the descriptive material throughout the book, they make their treatment sufficiently interesting and alive to stimulate the attention of the better-prepared students with professional aims. The care with which the content has been chosen is reflected in the list of "references for further reading" at the end of each chapter. These have been selected from the large mass of chemical books and magazine articles, with the maturity of the freshman student in mind, and include items published just before the book went to press. By means of this extensive and well-chosen bibliography the student is encouraged to start his acquaintance with the vast literature of chemistry and to enlarge his knowledge beyond the scope of the textbook.

The treatment of modern chemical theories is thoroughly up to date. This is not surprising, since the authors have been at the forefront in the recent renaissance of inorganic chemistry in this country. The atomic bomb, however, has received what is probably the least hysterical account ever published on the subject. The topic upon which so many millions of words have been published since 6 August 1945 has been accorded fewer than 400! One may surmise that these were interpolated into the galley at the last moment and that in future editions there will be some expansion of this revolutionary topic.

It is hoped that this book will receive the wide acceptance that it deserves as it represents a genuine advance in textbooks for the general college course.

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